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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,905	07/25/2003	Guido Franzoso	21459-94575	2235

7590 11/29/2006

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EXAMINER	
JOYCE, CATHERINE	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,905	FRANZOSO ET AL.	
	Examiner	Art Unit	
	Catherine M. Joyce	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *3-5 and 7-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. The Amendment filed August 30, 2006 in response to the Office Action of March 30, 2006, including the Declaration by Guido Franzoso under 37 CFR § 1.132, is acknowledged and has been entered. Previously pending claims 1, 2 and 6, and newly added claims 36 and 37 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are being maintained:

Claim Rejections - 35 USC 112

4. Claims 1, 2 and 6 remain rejected under 35 USC 112, first paragraph, and claims 35 and 36 are newly rejected under 35 USC 112, for the reasons set forth previously in the Paper mailed August 30, 2006, Section 1, pages 5-10. **(enablement)**

Applicant argues that the specification shows that there is a physical interaction between Gadd45β and kinases in the JNK pathway in 293 cells, that Gadd45β inhibits JNKK2 activity in vitro, that Gadd45β inhibits JNKK2 activity in 3DO cells, that distinct polypeptide regions in JNKK2 and Gadd45β interact, wherein these data illustrate that Gadd45β modulates the JNK pathway by regulating JNKK2 activity. Applicant further argues that the Franzoso Declaration demonstrates that Gadd45β modulation of the JNK pathway extends to in vivo models because the Declaration provides data that demonstrate that Gadd45β knock-out mice show that JNK activation leads to cell death in mice following hepatectomy. Applicant further argues that the specification discloses an agent, e.g. a cell permeable peptide that includes a Gadd45β binding region on JNKK2 activates cell death and thereby modulates JNK activity. Applicant further argues that there are no claims drawn to the treatment of cancer and therefore the lack of enablement discussion for the treatment of cancer was not on point. Applicant further argues that the PTO is not the FDA and it is the FDA's role to decide if cancer therapies are effective.

Applicant's arguments have been considered but have not been found to be persuasive. Applicant's arguments that the Franzoso Declaration data using Gadd45β knock-out mice and showing that JNK activation leads to cell death in mice following hepatectomy demonstrates that Gadd45β modulation of JNK pathway extends to in vivo models are not found to be persuasive because data is not commensurate in scope with the claimed invention for the following reasons: (i) the data does not show the treatment of any disease, as is contemplated by the specification and is encompassed by the broadly drawn claims, and (ii) the data does not show the use of an agent that interacts with Gadd45β is effective in vivo, but rather shows physiological effects of complete Gadd45β gene knock-out. Thus, in view of the teaching set forth in the specification and further considering the data provided in the Franzoso declaration, one of skill in the art would not predict that the invention would function as claimed in vivo in the treatment of any disease, for example cancer, for the reasons set forth in the previous Office Action. Although, none of the claims are drawn specifically to the treatment of cancer, the treatment of cancer is encompassed by the broadly drawn claims and is clearly contemplated in the specification. The Examiner is cognizant of the fact that the PTO is not the FDA and that it is the FDA's role to decide if cancer therapies are effective. However, an enablement inquiry under 35 USC § 112, as was applied in this case, is in the purview of the PTO. Thus, the claims remain rejected for the reasons set forth in the previous Office Action.

5. Claims 1, 2 and 6 remain rejected under 35 USC 112, first paragraph, under 35 USC 112, first paragraph, and newly added claims 36-37 are rejected under 35 USC 112, first paragraph, are for the reasons set forth previously in the Paper mailed August 30, 2006, Section 2, pages 10-13. **(written description).**

Applicant argues that the pending claims are to a method and not a molecule, and thus presumably Applicant argues that the previously stated written description is not applicable to a method claim. Applicant further argues that the claims have been amended. Applicant further argues that the specification as filed disclosed a working

example of a peptide that can modulate the JNK pathway and regulate cell death and further describes other agents such as anti-sense, ribozymes, and mimetics that are capable of modulating the JNK pathway by interfering with the Gadd45β-JNK interaction.

Applicant's arguments have been considered but have not been found to be persuasive. Applicants arguments that the pending claims are drawn to a method and not a molecule are not found to be persuasive because, as specifically stated in the previous Office Action, a disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product. Applicant's argument that the claims have been amended are not found be persuasive because the amendments to the claims do not appear to impact the written description analysis and Applicant does not specifically argue any claim amendments or point out how such amendments would affect the written description analysis. Applicant's argument that the specification as filed disclosed a working example of a peptide that can modulate the JNK pathway and regulate cell death and further described other agents such as anti-sense, ribozymes, and mimetics that are capable of modulating the JNK pathway by interfering with the Gadd45β-JNK interaction are not found to be persuasive because the specification structurally describes only one agent, and HIV-TAT-Peptide 1 fusion, that was capable of functioning as claimed and thus necessarily fails to describe a representative number of species that function as claimed, or structural features common to members of the genus, or a correlation between structure and function for members of the genus. Thus, the claims remain rejected for the reasons set forth in the previous Office Action.

6. Claims 1, 2 and 6 remain provisionally rejected under the judicially created doctrine of double patenting as being unpatentable over claims 1-2, and 6 of U.S. Application SN 10/263330 for the reasons set forth previously in the Paper mailed August 30, 2006, pages 14-15.

Applicants state that if pending claims are found to be allowable, Applicants will timely file terminal disclaimers to overcome the provisional double patenting rejection in view of U.S. Serial No. 10/263330. Thus, the provisional double patenting rejection is maintained of record.

New Grounds of Rejection

Claim Rejections - 35 USC 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 36 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36 and 37 are objected to in the recitation of the limitation "the peptide". There is insufficient antecedent basis for this limitation in the claims.

Claim 1 is objected to in the recitation of the term "interacts". This term is not defined by the claim or the specification and one of skill in the art would not be apprised of the metes and bounds of the claim.

Claims 36 and 37 are objected to as being indefinite in that it is not clear if a peptide that comprises the entire length of amino acids 132-156 (claim 36) or the entire length of amino acids 220-234 (claim 37) is intended, or whether any portion of these specified amino acid sequence regions is intended. Thus, one of skill in the art would not be apprised of the metes and bounds of the claim.

Claim 1 is objected to in that it is unclear how the agent is to be used to increase JNK activation. Thus, one of skill in the art would not be apprised of the metes and bounds of the claim.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 37 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claim is as follows:

a method for increasing JNK activation leading to programmed cell death, said method comprising:

(a) selecting an agent that interacts with Gadd45β; and

(b) using the agent to increase JNK activation,

wherein

(a) the agent is sufficient to block the suppression of JNK activation by Gadd45β; and

(b) contacting cells with said agent to increase the percent of cells that undergo programmed cell death,

wherein the peptide comprises an amino acid sequence from positions 220-234 of SEQ ID NO:50, wherein the sequence is GKMTVAIVKALYYLK (claim 37).

The specification teaches as set forth in the previous Office Action. The specification also teaches at paragraph 000150 that while Peptide 1 (comprising the amino acids 132-156) prevented MKK7 (i.e. JNKK2) inhibition by Gadd45β, Peptide 7 (comprising the amino acid 220-234) did not show this activity. The specification also teaches a paragraph 000151 that while a HIV-TAT-Peptide 1 fusion that was transduced into cells markedly increased susceptibility of cells to TNF-α, Peptide 7 fusions had no effect on apoptotic response to TNF-α.

The teaching of the specification cannot be extrapolated to enable the claims because, in view of the demonstration in the specification of a lack of biological effect of the peptide comprising the sequence GKMTVAIVKALYYLK, i.e. Peptide 7, one of skill in the art would not predict that the invention would function as claimed.

11. All other objections and rejections recited in the previous Office Action are hereby withdrawn.

12. No claims allowed.

13. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Catherine M. Joyce whose telephone number is 571-272-3321. The examiner can normally be reached on Monday thru Friday, 10:15 - 6:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8700.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Catherine M. Joyce
Examiner
Art Unit 1642

SUSAN UNGAR, PH.D
PRIMARY EXAMINER